Clinical Update

Naval Postgraduate Dental School
National Naval Dental Center
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Bethesda, Maryland 20889-5602

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Leishmania

Captain Mikelle Kuehn, USAF, DC and Commander James Castle, DC, USN

Background

Skin conditions and infections have been a common problem within the U.S. military population, particularly during and soon after times of deployment.[1] With the recent increase in troop deployment to the Middle East and Persian Gulf regions, concern over cutaneous leishmaniasis has also increased as military personnel return to the U.S. with the disease. Interestingly, trends in leishmania infection in military personnel can be seen from World War II through the Gulf War in 1990 and 1991, to the present operations in Iraq and Afghanistan. During World War II, a high incidence of leishmaniasis was seen among those deployed to the Persian Gulf, while the Gulf War saw very few cases reported out of the nearly 700,000 troops deployed to the same area. Only 12 cases of visceral leishmaniasis and 19 cases of cutaneous leishmaniasis resulting from Gulf War deployments were diagnosed. Decreased rates of infection are thought to be due to use of insect repellent and insecticides, the time of year (cooler weather), and troop location (the open desert as opposed to urban areas or oases where the primary rodent hosts reside.) [2,3]

In contrast to the Gulf War, the present conflict in Iraq has garnered 522 documented cases of cutaneous leishmaniasis in military personnel deployed to SW and Central Asia between August 2002 and February 2004.[4] Military pathologists are gaining valuable experience in the diagnosis of the disease, however it is equally important that military clinicians be able to identify potential leishmaniasis cases and to include the disease within an appropriate differential diagnosis. It is possible that a military dentist may be the first clinician to evaluate a patient with leishmaniasis as mucocutaneous leishmaniasis may be the initial or only presenting sign.[5]

Life Cycle

Leishmania is endemic in nearly 90 countries, and presents clinically in two general forms, visceral or cutaneous. Leishmania is a protozoal parasite with numerous species, more than 20 of which are known to cause human infection.[2] The parasite exists initially as a motile form within an insect vector: sandfly genus Phlebotomus in the Middle East, and genus Lutzomyia in South and Central America. Over a period of 10 days the infectious, non-motile form develops, subsequently transferring to the host through the bite of the sandfly. Host macrophages ingest the invaders, although leishmania are adapted to survive acidic environments and so they remain within the macrophages as obligate intracellular parasites.[2,5] Sandflies breed within organic wastes including feces and leaf litter, and they can be found near rodent and human habitats in endemic areas.[2] The insects unfortunately can pass through most mosquito netting. While the sandfly is the primary mode of transmission, other routes of transmission are possible including via sexual intercourse, blood transfusion, and congenital transmission.[5]

Clinical Presentations

Cutaneous leishmaniasis infection encompasses four variants: cutaneous, recurrent (hyperergic), diffuse (anergic), and mucocutaneous. The diffuse type arises in patients that lack a specific cellular immune response, as in HIV patients. A variant of the visceral form, post-kala-azar leishmanoid, can occur several years after resolution of visceral infection and presents as various skin lesions. This form is usually fatal within a few years.[1,2,3]
The general clinical course of cutaneous leishmaniasis involves an incubation period of two to eight weeks and possibly longer. After incubation, solitary or multiple erythematous papules develop at the site of the original bite. The papules increase in size to become nodules that eventually ulcerate. The ulcers often are large and painless, with distinct, firm, raised borders and a central granulating depression. Depending upon the specific infecting species, healing usually spontaneously occurs anywhere between one and several years later even without treatment, leaving a depressed, cribriform scar.[1,2]

Mucocutaneous leishmaniasis (MCL) occurs in approximately 5% of patients with a history of cutaneous infection, arising when the parasites spread via lymph or blood from the skin to the mucosa within weeks of the initial bite. Ulcers can develop on pharyngeal, oral, and nasal mucosa and often do not present until several years after resolution of other cutaneous lesions. Unlike the cutaneous lesions, mucosal ulcers will not spontaneously regress, but instead progress to destroy skin, mucosa and cartilage of the larynx, pharynx, nasal septum, palate, and lips. [1,2,5]

Visceral leishmaniasis patients present with enlargement of the liver and spleen, pancytopenia (decreased numbers of all blood cell types), weight loss, and high fever. Patients with visceral leishmaniasis (also known as kala-azar) characteristically will not feel ill even while presenting with a high fever. [1,2,3]

Diagnosis

Several methods may be employed in the diagnosis of cutaneous leishmaniasis, including skin scraping of lesions, punch biopsy, needle aspiration, and immunological tests. The procedure recommended for skin scraping involves the administration of local anesthesia followed by crust removal and cleaning of the ulcer. Scrapings should be taken both from the margin of the lesion and from the center, then smeared on five slides to be sent to a pathologist for a Giemsa stain. Punch biopsies should include 3 mm of tissue along the active border of the lesion. Prior to placing the tissue in formalin, an impression smear of the tissue needs to be made. Excess blood is removed from the tissue and the connective tissue margin is then blotted on a slide forming an impression smear. The smear is then submitted for a Giemsa stain. Immunologic tests include serum detection of host antibodies against leishmania, which works best in MCL, and polymerase chain reaction, which is highly specific but not always practical.

Diagnosis of MCL may be complicated due to delay in onset of the disease, as well as increased difficulty in identifying the mucosal parasites as compared with those found in cutaneous lesions.[1,2,6]

Treatment

Cutaneous leishmaniasis may need no treatment, however without treatment there is a risk for dissemination and development of mucosal disease.[2] Providing early treatment will usually cause lesions to heal more quickly and will prevent relapse. Some indications for early treatment include an immunocompromised patient, mucosal disease, and lesions that are unsightly, chronic, large, multiple, or lesions that are located over joints.[2] The pentavalent antimonial agent sodium stibogluconate (Pentostam) is the treatment of choice within the U.S., with a reported cure rate of 94% for cutaneous disease and 75% for MCL. Recommended dosage is 20 mg per kg body weight per day for 20 days. The drug does have reported reversible side effects including myalgia, arthralgia, elevation of liver enzymes, anemia, and fatigue. More adverse reactions may be seen in patients that are compromised in some way (elderly, pregnant, immunocompromised, etc.). Cures have also been reported using intralesional injections of sodium stibogluconate in conjunction with IV Pentostam.[1,2,5,7,8]

Prevention

While it is difficult to avoid the sandfly in endemic areas, there are ways to reduce contact with the infecting agent. Development of a vaccine is in progress and is comprised of the killed motile form of leishmania. Insecticides have been shown to reduce the sandfly population in urban areas, and destroying rodent reservoirs has decreased leishmania infection to a limited extent. To date, the most important factor in reducing infection among the deployed military population has been use of permethrin-treated uniforms and bed-nets, which have proven to be 75% effective in protecting soldiers from sandfly bites.[1,2]

Conclusion

Military dentists and physicians treat a specialized population of patients, namely active duty military personnel. The active duty population is at times placed in environments very different from those found in North America, and so will be exposed to diseases like leishmaniasis that are not commonly seen within the United States. Because of the current concern over the disease, the Armed Forces Institute of Pathology's Division of Infectious and Tropical Diseases Pathology has created a website for clinicians and pathologists to aid in the diagnosis, treatment, and reporting of cutaneous leishmaniasis:
http://www.afip.org/Departments/infectious/lm/ [6]

Concern over leishmaniasis is rapidly growing as more troops deploy to and return from Iraq and Afghanistan. The importance of anticipating and recognizing the disease cannot be overstated.

References

1. Jappe U. Unusual Skin Infections in Military Personnel. Clin Dermatol. 2002 Jul-Aug;20(4):425-34.
2. Markle WH, Makhoul K. Cutaneous Leishmaniasis: Recognition and Treatment. Am Fam Physician. 2004 Mar 15;69(6):1455-60.
3. Oumeish OY, Oumeish I, Parish JL. Gulf War Syndrome. Clin Dermatol. 2002 Jul-Aug;20(4):401-12.
4. Centers for Disease Control. Update: Cutaneous Leishmaniasis in U.S. Military Personnel---Southwest/Central Asia, 2002-2004. MMWR 2004;53(12);264-65.
5. Costa JW Jr, Milner DA Jr, Maguire JH. Mucocutaneous leishmaniasis in a US citizen. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003 Nov;96(5):573-7.
6. Kelly CC. AFIP experts provide rapid Leishmaniasis diagnosis in soldiers deployed to Iraq. AFIP Letter 2004;162(2):3.
7. Motta AC, Arruda D, Souza CS, Foss NT. Disseminated mucocutaneous leishmaniasis resulting from chronic use of corticosteroid. Int J Dermatol. 2003 Sep;42(9):703-6.
8. Czerniski R, Gilead L, Abedelmajeed N, Markitziu A. Intralesional therapy of oral leishmaniasis Int J Dermatol. 2003 Sep;42(9):752-4.

Dr. Kuehn is a first-year resident in the Oral and Maxillofacial Pathology program and Dr. Castle is Chairman of the Oral & Maxillofacial Pathology Department at the Naval Postgraduate Dental School.